February 8, 2006

M.R. (Chip) Witcher, CIH
Staff Industrial Hygienist
TSCA Coordinator
Syngenta Crop Protection, Inc.
410 Swing Road
Greensboro, NC 27409

Dear Mr. Witcher:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for Isophthalonitrile, posted on the ChemRTK HPV Challenge Program Web site on October 6, 2005. I commend Syngenta Crop Protection, Inc. for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Syngenta Crop Protection, Inc. advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission. Please send any electronic revisions or comments to the following e-mail addresses: oppt.ncic@epa.gov and chem.rtk@epa.gov.

If you have any questions about this response, please contact Mark Townsend, Chief of the HPV Chemicals Branch, at 202-564-8617. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

/s/

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: W. Penberthy
J. Willis

EPA Comments on Chemical RTK HPV Challenge Submission:
Isophthalonitrile

Summary of EPA Comments

The sponsor, Syngenta Crop Protection, Inc., submitted robust summaries to EPA for Isophthalonitrile (CAS No. 626-17-5) dated September 16, 2005. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 6, 2005.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitter needs to indicate whether certain of these endpoints are measured or estimated. If estimated, the submitter needs to provide measured data.

2. Environmental Fate. The submitter needs to provide estimated or measured data for the photodegradation endpoint and measured data for the stability in water and biodegradation endpoints. For fugacity modeling, appropriate measured input values are needed.

3. Health Effects. EPA reserves judgement on the adequacy of data for the gene mutations and developmental toxicity endpoints. The submitter needs to address deficiencies in the robust summaries.

4. Ecological Effects. Adequate data are available for toxicity to fish for the purposes of the HPV Challenge Program. The submitter needs to provide adequate data for the invertebrates and algal toxicity endpoints and address deficiencies in the robust summaries.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments on the Isophthalonitrile Challenge Submission

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, water solubility, and partition coefficient)

Adequate data are available for melting point and partition coefficient for the purposes of the HPV Challenge Program.

The submitter provided limited information from MSDSs in the robust summaries for boiling point, vapor pressure, and water solubility. The submitter needs to verify that these data are measured or else provide measured data to address these endpoints. Estimated data are not adequate for the purposes of the HPV Challenge Program because the use of estimated values introduces uncertainties that become magnified in modeling applications. Data from published sources are acceptable, as long as the submitter identifies the source(s).

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitter's proposal to provide only modeling data for all endpoints (as indicated on page 3 of the test plan) is not adequate for the purposes of the HPV Challenge Program.

Photodegradation. Estimated or measured photodegradation data are adequate for the purposes of the HPV Challenge Program.

Stability in water. The submitter needs to provide measured stability in water (hydrolysis) data following OECD Guideline 111.

Biodegradation. The submitter needs to provide measured ready biodegradation data following OECD Guideline 301.

Fugacity. EPA agrees that Level III modeling data will address the fugacity endpoint. However, the submitter needs to input appropriate measured values to develop these data. The use of estimated values introduces uncertainties that then become magnified in modeling applications.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data for acute, repeated-dose, chromosomal and reproductive toxicity are adequate for the purposes of the HPV Challenge Program. EPA reserves judgement on the adequacy of data for the gene mutation and developmental toxicity endpoints pending the submission of additional information.

Genetic Toxicity (gene mutations). The submitter needs to provide the response of the positive controls to validate the negative results of the assay.

Developmental toxicity. No robust summary data were submitted for this endpoint. The submitter concludes from the combination 28-day repeated-dose toxicity and one-generation rat reproduction study that there was no obvious/gross teratogenicity. The submitter needs to provide a separate robust summary for the developmental toxicity endpoint highlighting pertinent study parameters, with the following additional information: gross abnormalities, sexes of the litter, litter size, litter weights, post-natal growth of offspring, number of implantations, number of corpora lutea. EPA encourages the submission of an adequate study on an appropriate analog, if available, to strengthen the analysis for this endpoint.

Ecological Effects (fish, invertebrates, and algae)

The submitted data for fish toxicity are adequate for the purposes of the HPV Challenge Program. No data were submitted for the invertebrate toxicity endpoint and the algal toxicity robust summary has a reliability code of 4 (unassignable). The submitter needs to provide adequate measured data for the invertebrate and algae toxicity endpoints.

Specific Comments on the Robust Summaries

Health Effects

Genetic Toxicity (gene mutations). The submitter needs to include the responses of the positive and negative controls in the robust summaries.

Ecological Effects

Fish. The method cited should be OECD TG 203, not 403.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.